

Table 2.3 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Purdie <i>et al.</i> (1995), Queensland, New South Wales, Victoria, Australia, 1990–93	824 incident cases diagnosed and registered in all major gynaecological-oncology treatment centres in 3 states, aged 18–79 years; independent pathological confirmation of diagnosis; 860 population-based controls selected randomly from electoral rolls, stratified by age and geographical region	Interviewer-administered standardized questionnaire in clinic (cases) or home (some cases, all controls); information collected on medical, reproductive, family and occupational histories, as well as dietary factors and history of talc use	Use of talc around the abdomen or perineum	[467] 56.7%	1.3 (1.0–1.5)	Parity; other potential confounders, e.g. contraceptive use, also considered	
Shushan <i>et al.</i> (1996), Israel, 1990–93	200 incident cases (164 invasive, 36 borderline) diagnosed and reported to Israel Cancer Registry, aged 36–64 years; histological confirmation of diagnosis; 408 population-based controls selected by random-digit dialing; matched by geographical area	Interviewer-administered standard questionnaire; information collected on reproductive history, use of oral contraceptives and fertility drugs, exposure to talc; exposure to talc stratified into 'never/seldom', 'moderate/a lot'	<i>Use of talc</i> Moderate/a lot	21	[1.97] (<i>p</i> = 0.04)	No control for confounding	Study limited by the very sparse information on talc use and the unavailability of adjusted results for the association between use of talc and the risk for ovarian cancer

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Chang & Risch (1997), metropolitan Toronto and southern Ontario, 1989–92	450 incident cases (primary, invasive and borderline); aged 35–79 years; histological confirmation of diagnosis; 564 population-based controls identified through provincial records of all homeowners, tenants and family members; randomly selected from same residential area; matched by age within 15-year age groups	Interviewer-administered questionnaire; information collected on menstrual and reproductive history, use of hormones and oral contraceptives, and use of talc; exposure to talc categorized on basis of ‘any’ exposure, type of exposure, frequency and duration of perineal application	<p>‘Any’ exposure to talc</p> <p>Type of exposure</p> <p>Sanitary napkins</p> <p>After bathing</p> <p>Frequency of after-bath use (times/month)</p> <p>None</p> <p><10</p> <p>10–25</p> <p>>25</p> <p>Per 10 applications per month</p> <p>Duration of after-bath use (years)</p> <p>None</p> <p><30</p> <p>30–40</p> <p>>40</p> <p>Per 10 years of use</p>	<p>198</p> <p>51</p> <p>172</p> <p>76</p> <p>54</p> <p>41</p> <p>60</p> <p>71</p> <p>41</p>	<p>1.4 (1.1–1.9)</p> <p>1.3 (0.9–2.0)</p> <p>1.3 (1.0–1.7)</p> <p>1.0</p> <p>1.8 (1.2–2.7)</p> <p>1.1 (0.7–1.7)</p> <p>1.0 (0.6–1.5)</p> <p>0.9 (0.7–1.1)</p> <p>1.0</p> <p>1.7 (1.1–2.6)</p> <p>1.4 (1.0–2.2)</p> <p>0.9 (0.5–1.4)</p> <p>1.1 (1.0–1.2)</p>	<p>Age at interview, duration of oral contraceptive use, parity (number of full-term pregnancies), duration of lactation per pregnancy, history of tubal ligation or hysterectomy, family history of breast or ovarian cancer</p>	<p>Authors do not specify whether cases were identified through a cancer registry or some other reporting mechanism.</p> <p>Borderline significant trend observed with increasing duration of exposure to talc, but not with increasing frequency of exposure</p>

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Cook <i>et al.</i> (1997) Western Washington State, USA, 1986–1988	313 incident cases (234 invasive, 79 borderline) identified from records of Cancer Surveillance System of western Washington; white residents of three counties (King, Pierce, Snohomish), aged 20–79 years; no information on whether diagnosis was histologically confirmed; 422 white population-based controls selected by random digit-dialling (part of a larger control pool for several studies of cancer in women); matched by age	Structured in-person interviews; information collected on medical and reproductive histories, smoking habits, birth control methods and use of genital powders and deodorant sprays; exposure to genital powders assessed on the basis of ‘any’ lifetime exposure, method of use and cumulative lifetime exposure (days, months or lifetime applications)	<i>Lifetime perineal application</i>			Adjusted for age	
			None	154	1.0		
			Any	159	1.5 (1.1–2.0)	Adjusted for age	
			<i>Exclusive use of powder for</i>				
			Perineal dusting	55	1.8 (1.2–2.9)		
			Diaphragm storage	22	0.8 (0.4–1.4)		
			Dusting sanitary napkins	12	1.5 (0.6–3.6)		
			Deodorant spray	18	1.5 (0.8–3.0)	Adjusted for age and other methods of genital powder application	
			<i>Any use of powder for</i>				
			Perineal dusting	95	1.6 (1.1–2.3)		
			Diaphragm storage	46	1.0 (0.6–1.6)		
			Dusting sanitary napkins	38	0.9 (0.5–1.5)		
			Deodorant spray	40	1.9 (1.1–3.1)	Adjusted for age and other methods of genital powder application	
			<i>Cumulative lifetime perineal dusting (days)</i>				
			None	154	1.0		
			≤2000	20	1.8 (0.9–3.5)		
			2001–5000	24	1.6 (0.9–2.9)		
			5001–10 000	21	1.2 (0.6–2.4)		
			>10 000	28	1.8 (0.9–3.4)		

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Eltabbakh <i>et al.</i> (1998), Buffalo, NY, USA, 1982–96	‘Study’ group: 50 women admitted for treatment of primary extra-ovarian peritoneal cancer to Roswell Park Cancer Institute; histological confirmation of diagnosis; ‘control’ group: 466 women treated for primary ovarian cancer at same centre; pathological review of diagnosis	Self-administered, 44-item questionnaire completed at hospital admission	Perineal use of talc	224 (48.1%)	$p=0.003$	No control for confounding	‘Cases for this study were women diagnosed with primary peritoneal cancers. Case definition excluded patients with diagnoses of peritoneal mesothelioma, borderline tumours of peritoneum or invasive ovarian cancer; no healthy controls enrolled in this study. ‘Controls’ were women diagnosed with primary epithelial ovarian cancer. Control definition excluded patients with diagnoses of non-epithelial ovarian cancer and ovarian cancer secondary to metastases from other sites.

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Godard <i>et al.</i> (1998), Montreal, Quebec, Canada, 1995– 96	170 incident cases with primary invasive or borderline epithelial tumours, identified at two gynaecological clinics, aged 20–84 years; histological confirmation of diagnosis; 170 population-based controls selected by a modified random-digit dialling method; frequency-matched by age (± 1 year), French Canadian ethnicity	Standardized 57-item questionnaire; telephone or in-person interviews conducted with cases, no information on how controls were interviewed; qualitative assessment of perineal talc exposure (ever/never)	'Ever' use of talc on perineum	[18] (10.6%)	2.5 (0.9–6.6)	Age at menarche, age at menopause, parity, age at first and last childbirth, duration of oral contraceptive use, age at last oral contraceptive use, tubal ligation, alcohol use, previous breast or abdominal surgery	

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Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Cramer <i>et al.</i> (1999), eastern Massachusetts and New Hampshire, USA, 1992–97	563 incident cases (including borderline tumours) identified through hospital tumour boards or statewide cancer registries; age range not provided; histological confirmation of diagnosis for all cases; 523 population-based controls selected by random-digit dialling and through annual listings of names, ages and addresses of all Massachusetts residents (women over the age of 60 years); frequency-matched by age (± 4 years), location of residence	In-person interviews using standardized questionnaire; information collected on medical and reproductive histories, family history and personal habits; multiple questions on potential routes of talc exposure (non-genital, genital, husband's use), brands used, age at first use, duration and frequency of use	No genital exposure Any genital exposure <i>Method of use</i> No use Non-genital areas Dusting Dusting perineum Dusting sanitary napkins Dusting underwear More than one method <i>Frequency (uses/month)</i> None <30 30–39 ≥40 <i>Duration of use (years)</i> None <20 20–30 >30	411 152 312 99 71 20 8 53 312 64 59 23 312 55 32 59	1.0 1.6 (1.2–2.1) 1.0 1.1 (0.8–1.5) 1.5 (1.0–2.2) 1.5 (0.7–3.1) 1.2 (0.4–3.6) 2.2 (1.3–3.6)	Age, study site, parity, oral contraceptive use, body mass index, family history of breast or ovarian cancer, history of tubal ligation	

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Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Cramer <i>et al.</i> (1999) (contd)	<i>Total no. of applications</i>		None	312	1.0		
			<3000	51	1.8 (1.1–3.0)		
			3000–10 000	36	1.4 (0.8–2.4)		
			>10 000	59	1.4 (0.9–2.2)		
			<i>p</i> for trend		0.16		
	<i>Total no. of applications (censored analysis)</i>		None	312	1.0		Censored analysis excludes talc applications that occurred during non- ovulatory years or after hysterectomy or tubal ligation. Includes non- genitally exposed women.
			<3000	59	1.5 (1.0–2.4)		
			3000–10 000	51	1.7 (1.1–2.8)		
			>10 000	36	1.8 (1.0–3.2)		
			<i>p</i> for trend		0.02		

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Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Wong <i>et al.</i> (1999) Buffalo, NY, USA, 1982–92	462 incident cases admitted for treatment of primary extra-ovarian peritoneal cancer to Roswell Park Cancer Institute, mean age, 54.9 years; histological confirmation of diagnosis; 693 hospital-based controls treated for non-gynaecological malignancies at same cancer centre; mean age, 54.9 years; frequency-matched to cases by age at diagnosis (± 5 years)	Self-administered, 44-item questionnaire completed at hospital admission; information collected on medical, social, family, dietary and occupational histories; method of talc use (never, sanitary napkin, genital/thigh area, both) assessed and duration of use	<i>Method of use</i> Never Sanitary napkin Genital or thigh area Both <i>Duration of use (years)</i> None 1–9 10–19 ≥ 20	241 13 157 51 241 39 49 101	1.0 0.9 (0.4–2.0) 1.0 (0.8–1.3) 1.1 (0.7–1.7) 1.0 0.9 (0.6–1.5) 1.4 (0.9–2.2) 0.9 (0.6–1.2)	Age, parity, oral contraceptive use, smoking, family history of ovarian cancer, age at menarche, menopausal status, income, education, geographical location, history of tubal ligation or hysterectomy	Case population largely that reported by Eltabbakh <i>et al.</i> (1998); 32 cases, 39 controls did not recall duration of use.

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Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Ness <i>et al.</i> (2000), eastern Pennsylvania, southern New Jersey, Delaware, USA, 1994–1998	767 incident cases identified at 39 hospitals in the Delaware Valley region; aged 20–69; diagnosis within 6 months prior to interview; pathological review of a random subset of cases ($n = 120$) 1367 population-based controls identified through random digit dialing (≤ 65 years of age) and Health Care Financing Administration lists (65–69 years of age); frequency matched by age and location of residence	Standardized in-person interviews; information collected on sexual activity, use of contraceptives, menstrual and reproductive history, and history and duration of talc use (genital, non-genital applications, exposure via male sexual partners)	<i>Method of use</i>				
			Never	349	1.0	Age, parity, race, family history of ovarian cancers, oral	Risk for ovarian cancer compared with 50 women with primary peritoneal cancers; no control for confounding; analysis of duration examined risk for cases reporting use of talc on the feet, genital and rectal areas.
			Feet, arms, breasts	335	1.4 (1.1–1.6)		
			Genital/rectal	161	1.5 (1.2–2.0)	contraceptive use, tubal	
			Sanitary napkin	77	1.6 (1.1–2.3)	ligation, hysterectomy, lactation	
			Underwear	70	1.7 (1.2–2.4)		
			Diaphragm/cervical cap	10	0.6 (0.3–1.2)		
			Male partner	56	1.0 (0.7–1.4)		
			<i>Duration of use (years)</i>				
			Never	401	1.0		
			<1	17	2.0 (1.0–4.0)		
			1–4	76	1.6 (1.1–2.3)		
			5–9	40	1.2 (0.8–1.9)		
			≥ 10	233	1.2 (1.0–1.5)		

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Langseth & Kjaerheim (2004), Norway, 1953– 99	35 (invasive and borderline tumours) selected from cohort of 4247 female pulp and paper workers; cohort follow-up, 1953–99; histological review and confirmation of diagnosis; 121 selected from the cohort by incidence density sampling; matched by birth (year ±2 years); controls had no ovarian cancer and had intact ovaries	In-person interviews conducted at mills or by telephone; information collected on occupational history, household exposure to asbestos, menstrual and reproductive history, hereditary risk of cancer, as well as talc use on sanitary napkins, underwear or diapers or by husband in genital area.	‘Ever’ use of talc for personal hygiene	12	1.2 (0.4–3.2)	Adjusted for possible confounders, but not explicitly stated	Nested case-control study conducted in a cohort study of 10 pulp and paper mills; many missing values among proxy respondents

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Mills <i>et al.</i> (2004), central California, USA, 2000–01	249 incident cases from 22 counties diagnosed in two regional cancer registries, using rapid case ascertainment procedures; histological confirmation of diagnosis for a subset of cases; 1105 population-based controls identified by random-digit dialling; frequency-matched by age, race, ethnicity	Telephone interview to obtain information on medical history, menstrual and reproductive history, family history of cancer, history of perineal talc exposure (frequency, duration and calendar years of use); 'cumulative' use calculated by multiplying frequency (categorical variable) by duration in months	<i>Perineal use of talc</i> Never Ever <i>Frequency of use</i> Never <1/week 1–3/week 4–7/week <i>p</i> for trend <i>Duration of use (years)</i> Never ≤3 4–12 13–30 >30 <i>p</i> for trend <i>Cumulative use</i> Never 1st quartile (lowest) 2nd quartile 3rd quartile 4th quartile (highest) <i>p</i> for trend	143 106 143 34 31 41	1.0 1.4 (1.0–1.9) 1.0 1.3 (0.9–2.1) 1.6 (0.7–1.8) 1.7 (1.1–2.6) 0.015	Age, race/ethnicity, duration of oral contraceptive use, breastfeeding. Additional covariates considered to be potential confounders included family history of breast or ovarian cancer, parity, history of pregnancy, body mass index, hysterectomy, tubal ligation, duration of post-menopausal use of hormones.	Cumulative use calculated as frequency (categorical weighting from 0–3) multiplied by duration.
				143 18 32 29 21	1.0 1.0 (0.6–1.8) 1.9 (1.2–3.0) 1.5 (0.9–2.3) 1.2 (0.7–2.1) 0.045		
				143 18 28 34 20	1.0 1.0 (0.6–1.8) 1.8 (1.1–3.0) 1.7 (1.1–2.7) 1.1 (0.6–1.8)		
					0.051		

CI, confidence interval

to talc by way of contraceptives, perineal hygiene or surgery. Ninety-two cases (42.8%) and 61 controls (28.4%) reported a history of regular use of talc as a dusting powder to the perineum, on sanitary napkins or on both. After adjustment for parity (yes/no) and menopausal status (pre-/post-), a significant association was found between 'any perineal use' of talcum powder and the risk for ovarian cancer (odds ratio, 1.9; 95% CI, 1.3–2.9). This association was attenuated but still significant after adjustment for additional potential confounders, including religion, marital status, level of education, weight, age at menarche, parity (number of children), oral contraceptive use, menopausal use of hormones and tobacco smoking (adjusted odds ratio, 1.6; 95% CI, 1.0–2.5). A single type of perineal exposure to talc (either as a dusting powder to the perineum or on sanitary napkins) was associated with a borderline significantly increased risk for ovarian cancer (odds ratio, 1.6; 95% CI, 1.0–2.5) after adjustment for parity and menopausal status, while a history of both types of perineal exposure was associated with a significant increase in risk (adjusted odds ratio, 3.3; 95% CI, 1.7–6.4). No association was seen between other potential sources of exposure to talc (pelvic surgery, use of condoms, use of diaphragm or using talc for diaphragm storage) and the risk for ovarian cancer. In addition, the results were essentially unchanged after excluding women who had had a tubal ligation or hysterectomy (odds ratio, 2.8; $P < 0.003$), although the authors noted that these surgical procedures are usually performed at mid-life when substantial exposure to talc may already have occurred. The distribution of tumour histologies was similar for exposed and unexposed cases; 53.7% of tumours were classified as serous among the unexposed cases and 48.9% among the exposed cases with 'any' perineal use of talc. [Limitations of this report include the lack of information on duration and frequency of talc use. In addition, participation rates among the controls were quite low (50%), although the authors noted in a secondary analysis that, when cases were matched to the first control selected (i.e. 100% participation), a positive association was also found (odds ratio, 2.44; $P < 0.05$).]

Hartge *et al.* (1983) published a brief report of a study conducted between 1974 and 1977 in the Washington DC (USA) area. The study included 197 cases treated for pathologically confirmed epithelial ovarian cancer at participating hospitals and 197 controls treated at the same hospitals for conditions other than pregnancy, malignancies and gynaecological or psychiatric diseases. Controls were frequency-matched to cases by age, race and hospital. Interviews were conducted in the hospital for controls and at home for most cases to collect information on reproductive and sexual history, medical history, drug use and other exposures. Questions on exposure to talc were added after the study began. As a result, the analysis included only 135 cases and 171 controls with information on exposure to talc. Sixty-seven cases [49.6%] and 100 controls [58.5%] reported 'any' use of talc (including non-genital uses), while seven cases [5.2%] and three controls [1.8%] reported genital use of talc (including use on genitals, on sanitary napkins or on underwear). No association was observed between 'any' use of talc and the risk for ovarian cancer (odds ratio, 0.7; 95% CI, 0.4–1.1). This estimate was unchanged after adjustment for race, age and pregnancy. A non-significant positive association was found between genital use of talc and the risk for ovarian cancer (odds

ratio, 2.5; 95% CI, 0.7–10.0). [Limitations of this study included its small size and the low prevalence of genital use of talc, the lack of information on its duration and frequency and age at first use, the lack of control for other potential confounders and the increased potential for selection bias due to different interviewing protocols for cases and controls. In addition, no information was given in this brief report on the methods used in the analysis to control for confounding.]

Whittemore *et al.* (1988) analysed the association between perineal use of talc and the risk for invasive epithelial ovarian cancer among 188 cases and 539 controls in the San Francisco Bay area (CA, USA). Cases were residents of northern California, aged 18–74 years, who had been diagnosed with an invasive ovarian tumour between January 1983 and December 1985 at one of eight hospitals. Controls were either selected from among women who had been hospitalized for a non-cancerous condition at one of these eight hospitals or were identified from the population using random-digit dialling. Women in each control group were matched to each case by age (within 5 years) and race (white, black, other), plus hospital and date of admission (within 3 months) for the hospital controls ($n = 280$) and telephone area code and prefix for the population-based controls ($n = 259$). Structured interviews were conducted in the homes of participants to obtain information on the history, frequency and duration of perineal use of talc, medical history and additional covariates of interest (menstrual and reproductive histories, family history and environmental exposures, such as consumption of alcohol, coffee and tobacco). Of 317 eligible cases, eight (2.5%) were excluded due to physician refusal, 30 (9.5%) due to patient refusal, 44 (13.9%) due to death or incapacitating illness and 47 (14.8%) due to non-invasive tumours, which left 188 (59.3%) for inclusion in the analysis. Among the controls, 68% of the women identified as eligible hospital controls ($n = 354$) and 71% of the women identified by telephone as eligible population-based controls ($n = 329$) agreed to participate. After excluding controls matched to cases with borderline tumours, 280 hospital controls and 259 population controls were included in the analysis (Wu *et al.*, 1988). Exposure to talc was categorized by type of application (perineum only, sanitary pads only, diaphragm only, any two types of application or all three types of application), duration of use before tubal ligation (none, 1–9 years, ≥ 10 years, unknown) and frequency of use (none, 1–20 applications per month, > 20 applications per month, unknown). Conditional logistic regression was used to calculate the odds ratio for each exposure and to test for trend. Ninety-seven cases (51.6%) and 247 controls (45.8%) reported previous use of talcum powder on the perineum to yield an odds ratio of 1.40 ($P = 0.06$) after adjustment for parity. Since the odds ratios were similar when hospital-based and population-based controls were analysed separately, analyses using the combined group of controls were reported. After adjustment for parity and oral contraceptive use, the odds ratio for use of talc on the perineum only was 1.5 (95% CI, 0.8–2.6). No significant associations were observed with either individual or multiple types of perineal talc use, including the combination of use on the perineum, sanitary napkins and a diaphragm (odds ratio, 1.4; 95% CI, 0.9–2.0 for any two types of use versus 0.4; 95% CI, 0.0–2.9 for all three types combined). No

significant trend was observed with duration of talc use on the perineum before tubal ligation or hysterectomy. Odds ratios were 1.6 (95% CI, 1.0–2.6) for 1–9 years of exposure and 1.1 (95% CI, 0.7–1.7) for more than 10 years of exposure. A non-significant trend of increased risk with increasing frequency of perineal use of talc was observed, with an overall odds ratio of 1.3 (95% CI, 0.9–1.9; $P = 0.19$) for 30 applications per month. When stratified by history of perineal use of talc (yes/no) and history of tubal ligation or hysterectomy (yes/no), women who had used talc perineally and but had not undergone surgery for sterilization had the highest risk for ovarian cancer (odds ratio, 1.3; 95% CI, 0.9–2.0). [Limitations of this study included the lack of information on talc use.]

Booth *et al.* (1989) reported results of a hospital-based case-control study of the risk for ovarian cancer conducted in 15 hospitals in London and Oxford (United Kingdom) from October 1978 to February 1983. Women aged 65 years or under at diagnosis and who were diagnosed within 2 years of the study interview were eligible for inclusion. A total of 280 potential cases were identified, interviewed and classified with respect to tumour histology. After excluding 45 women, 235 cases were included in the analysis. A total of 451 controls with the same age distribution as the cases were selected from the same 15 hospitals. Controls had a range of admission diagnoses; gastrointestinal disease ($n = 105$) and bone or joint disease ($n = 70$) were the most common. Women were excluded as controls if they had a history of bilateral oophorectomy or if they had a condition related to oral contraceptive use or other reproductive factors. Participation rates were not provided. Interviewers used a standard questionnaire to obtain information on reproductive and menstrual history, as well as exposure to exogenous estrogens, cigarettes and talc. Talc exposure was categorized according to the frequency of perineal use (never, rarely, monthly, weekly or daily) and whether it was used for storage of a diaphragm. Multiple logistic regression adjusted for age and socioeconomic status was conducted. Fifty-seven cases [24.3%] and 77 controls [17.1%] reported a history of weekly use of talc in the genital area, while 71 cases [30.2%] and 139 controls [30.8%] reported daily use. Weekly genital use of talc was associated with a significantly increased risk for ovarian cancer (odds ratio, 2.0; 95% CI, 1.3–3.4), while daily use was associated with a non-significant increase in risk (odds ratio, 1.3; 95% CI, 0.8–1.9), after adjustment for age and socioeconomic status. The p -value for trend with increasing frequency of use was of borderline significance ($P = 0.05$). The percentage of diaphragm users who reported storing their diaphragm in talc was not significantly different between the cases (86%) and controls (81%). [Limitations of this hospital-based study included the limited information on talc use. As participation rates were not provided, the possibility of selection bias is difficult to evaluate. Although covariates such as oral contraceptive use or parity were available, it was not explicitly stated if they were evaluated.]

Harlow and Weiss (1989) conducted a study of perineal use of powder and the risk for borderline ovarian cancer in western Washington State, USA. Cases were 116 Caucasian women aged 20–79 years who had been diagnosed with borderline serous or mucinous epithelial ovarian cancer between 1980 and 1985, and who were identified by International Classification of Diseases-0 codes obtained from a population-based

cancer-reporting system. Controls were identified from the same counties of residence by random-digit dialling. A total of 158 women with a similar age distribution to the cases and who had not undergone a bilateral oophorectomy were included in the analysis. Cases and controls were interviewed in-person to obtain information on reproductive, sexual and medical histories, as well as on perineal exposure to talc (through multiple open-ended questions about the history of powder use of the participant). Among all eligible cases and controls identified for the study, 68% of the cases and 74% of the controls were interviewed. The authors controlled for age (20–39, 40–59 or 60–79 years), parity (nulliparous or parous) and oral contraceptive use (ever/never). Exposure to talc was broadly categorized as ‘any perineal use of dusting powders’ (after bathing, on sanitary napkins or for diaphragm storage) and further subcategorized according to method of use (diaphragm storage only, after bathing only, sanitary napkins only, after bathing and on sanitary napkins and specific combinations of the various methods) and type of powder used (cornstarch only, baby powder only, talc unspecified (no combined use), deodorizing powder only or combinations of powders). Forty-nine cases [42.2%] and 64 controls [40.5%] reported a history of ‘any perineal exposure to powder’ to yield an odds ratio of 1.1 (95% CI, 0.7–2.1). When analysed by the type of powder used, the risk for borderline ovarian cancer was elevated only for perineal use of deodorizing powder alone (odds ratio, 3.5; 95% CI, 1.2–28.7) or in combination with other powders (odds ratio, 2.8; 95% CI, 1.1–11.7). No association was noted for the use of baby powder alone (odds ratio, 0.8; 95% CI, 0.4–1.9) or for combined use (odds ratio, 0.9; 95% CI, 0.5–2.0) or for other unspecified use of talc (odds ratio, 1.0; 95% CI, 0.4–2.4). No significant association was found between risk for borderline tumours and any individual method of powder use, including use after bathing, on sanitary napkins or for diaphragm storage. The authors reported no increase in risk with increasing number of days of powder use, although the data were not provided in the paper. [Limitations of this study included the incomplete information on powder use and its small size.]

Chen *et al.* (1992) (described in detail in Section 2.1.2) conducted a case–control study in Beijing, China, of several risk factors for epithelial ovarian cancer that included perineal exposure to talc (yes/no use of dusting powder to the lower abdomen or perineum for 3 or more months). The analysis was carried out on 112 newly diagnosed cases identified between 1984 and 1986 through the Beijing Cancer Registry and 224 age-matched community controls (two controls per case). Seven cases [6.3%] and five controls [2.2%] reported use of talc-containing powders which resulted in an odds ratio of 3.9 (95% CI, 0.9–10.6) after adjustment for education and parity. [The Working Group noted the incomplete ascertainment of cases of ovarian cancer due to the nature of the cancer-reporting system in China, the large number of cases that were excluded due to death and the exclusion of controls who had a history of serious health problems (which may have resulted in selection bias), the limited information on perineal use of talc, the lack of adjustment for other potential confounding variables, the small number of cases and the low prevalence of talc use.]

Harlow *et al.* (1992) analysed perineal exposure to talc and the risk for ovarian cancer among 235 cases and 239 controls in the Boston, MA metropolitan area (USA). Cases were diagnosed with ovarian cancer between June 1984 and September 1987 at one of 10 Boston hospitals and controls were identified from town registers listing the name, age and address of all residents in Massachusetts. All cases were Caucasian women aged 18–76 years at diagnosis and were similar to the controls with respect to race, age and area of residence. Of 397 cases identified during the study period, 31% were not interviewed due to physician and/or patient refusal, death or change of address. After excluding women whose cancer diagnosis was not confirmed by an independent pathology review [9.4% of eligible cases], 235 women were included in the analysis. A total of 526 women were contacted as potential controls. Of these, 239 [45.4%] were interviewed, 25% could not be reached, 10% reported a previous bilateral oophorectomy and 19% did not wish to participate in the study. In-person interviews were conducted with cases and controls to obtain information on occupational history, medical and reproductive histories, dietary history, cigarette smoking and hygienic practices (use of douches, types of sanitary protection used, perineal exposure to talc). Exposure to talc was categorized on the basis of ‘any’ exposure, the method of application (dusting on sanitary napkins and/or underwear, via partner or application to diaphragm, dusting on perineum), the brand used, age at first use, duration and frequency of use. Total lifetime exposure to talc was estimated by cumulating the frequency of exposure and years of use to arrive at a summary measure of the total number of applications (< 1000, 1000–10 000, > 10 000). Covariates evaluated as potential confounders included age, education, marital status, religion, weight, use of oral contraceptives and parity; of these, age, education (< 12 years, > 12 years), marital status (never/ever), religion (Jewish, non-Jewish), weight (< 140 lb, ≥ 140 lb) and parity (0, 1–2, > 2) were included in all multivariable models. A history of ‘any’ perineal exposure to talc-containing powders was reported by 48.5% of cases and 39.3% of controls to yield an odds ratio of 1.5 (95% CI, 1.0–2.1). When the method of application was examined, only direct application to the perineum as a dusting powder was associated with a significant increase in risk (odds ratio, 1.7; 95% CI, 1.1–2.7). Women who reported at least 30 applications of talcum powder per month had a significant increase in risk (odds ratio, 1.8; 95% CI, 1.1–3.0), while women with fewer applications per month did not. A significant positive trend was seen with number of monthly applications ($P = 0.046$). Women with at least 10 years of perineal exposure had a borderline significant increase in risk (odds ratio, 1.6; 95% CI, 1.0–2.7) and the p -value for trend was also of borderline significance ($P = 0.07$). Analyses stratified by age at first use indicated that women who first used talc genitally before the age of 20 years had the highest risk (odds ratio, 1.7; 95% CI, 1.1–2.7); those stratified by years since last use suggested that women with the most recent perineal use of talc (within the previous 6 months) had the highest risk (odds ratio, 2.3; 95% CI, 1.3–4.0). In an analysis stratified by use before versus after 1960, women who reported some perineal use of talc before 1960 had a significantly elevated risk for ovarian cancer (odds ratio, 1.7; 95% CI, 1.1–2.7), while women with exclusive genital use of talc after 1960 did not (odds ratio, 1.1;

95% CI, 0.6–2.1). Women who had used more than 10 000 lifetime applications had a borderline significant increase in risk (odds ratio, 1.8; 95% CI, 1.0–3.0). This was unchanged after excluding applications that occurred after tubal ligation or hysterectomy (odds ratio, 1.7; 95% CI, 1.0–3.0). However, when use of talc during non-ovulatory periods and after surgical sterilization was excluded, the increase in risk associated with more than 10 000 lifetime applications was significant (odds ratio, 2.8; 95% CI, 1.4–5.4). In analyses of each histological type and grade, the strongest associations were seen for endometrioid tumours (odds ratio, 2.8; 95% CI, 1.2–6.4) and tumours of borderline invasiveness (odds ratio, 2.4; 95% CI, 1.2–4.5) (Table 2.4).

Rosenblatt *et al.* (1992) conducted a hospital-based case-control study among 77 women who were hospitalized at Johns Hopkins Hospital in Baltimore, MD (USA) for ovarian cancer (cases) and 46 who were hospitalized for non-gynaecological, non-malignant conditions (controls). The cases were newly diagnosed with pathologically confirmed epithelial ovarian cancer between 1981 and 1985, the majority of whom were aged 40–69 years. Of 140 eligible cases, 108 (77.1%) were interviewed. Thirteen were subsequently excluded because no control was identified and 18 were excluded for an unspecified reason. Controls were matched to cases by age, race and date of diagnostic admission. Information on genital and respiratory exposure to fibre-containing substances (talc, asbestos and fibreglass), as well as potential confounders, was collected using a structured questionnaire which was administered in the hospital and by telephone. Covariates that were considered to be potential confounders included tobacco use, ‘ovulatory time period’, parity, family history of cancer, obesity, education, education of husband, previous history of cancer, marital status, religion and the use of oral contraceptives and other methods of contraception. Sources of genital fibre exposure (yes/no) included diaphragm use and dusting of either the perineum or sanitary napkins with talcum powder. Potential sources of respiratory fibre exposure (yes/no) included use of face or body powders containing talc, insulation installed at residence and living in the vicinity of or employment in a fibre-emitting industry (such as shipyard, asbestos or talc mine, asbestos/talc/fibreglass processing plant). A large percentage of both the cases (87%) and controls (88%) reported exposure to genital fibre, with an odds ratio of 1.0 (95% CI, 0.2–4.0) after adjustment for parity. A long duration of genital fibre use (median duration, ≥ 37.4 years) was associated with a borderline significant increase in the risk for ovarian cancer (odds ratio, 2.4; 95% CI, 1.0–5.8) after adjustment for religion. Odds ratios were also calculated for genital use of bath talc (odds ratio, 1.7; 95% CI, 0.7–3.9), use of talc on sanitary napkins (odds ratio, 4.8; 95% CI, 1.3–17.8) and use of talc on a diaphragm (odds ratio, 3.0; 95% CI, 0.8–10.8). No association was observed between risk for ovarian cancer and history of previous gynaecological or abdominal surgery that may have resulted in peritoneal exposure to talc. [Limitations of this study included the very small number of cases and controls, the broad definition of fibre exposure used in certain exposure variables and the limited information on perineal exposure to talc.]

Tzonou *et al.* (1993) conducted a hospital-based case-control study of risk factors for epithelial ovarian cancer in the Greater Athens region of Greece. The cases were 189 women

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Table 2.4. Perineal talc use and ovarian cancer risk: by tumour histology

References	No. of cases	Histology	Relative risk ^a (95% CI)
Harlow <i>et al.</i> (1992)	60	Serous ^b	1.4 (0.9–2.2)
	17	Mucinous	1.2 (0.6–2.5)
	18	Endometrioid	2.8 (1.2–6.4)
Chang & Risch (1997)	254	Serous ^b	1.3 (1.0–1.9)
	80	Mucinous	1.6 (1.0–2.6)
	74	Endometrioid	1.7 (1.0–2.8)
Cook <i>et al.</i> (1997)	131	Serous	1.7 (1.1–2.5)
	43	Mucinous	0.7 (0.4–1.4)
	36	Endometrioid	1.2 (0.6–2.3)
Cramer <i>et al.</i> (1999)	229	Serous invasive	1.7 (1.2–2.4)
	83	Mucinous	0.8 (0.4–1.4)
	130	Endometrioid/clear cell	1.0 (0.7–1.6)
Wong <i>et al.</i> (1999)	136	Serous	1.2 (0.7–2.1)
	11	Mucinous	1.5 (0.6–4.0)
	21	Endometrioid	1.4 (0.7–2.7)
Gertig <i>et al.</i> (2000)	76	Serous invasive	1.4 (1.0–1.9)
Mills <i>et al.</i> (2004)	42	Serous invasive	1.8 (1.1–2.8)
	10	Mucinous invasive	2.6 (0.9–7.4)
	14	Endometrioid	1.3 (0.6–2.6)

CI, confidence interval

^a Any or ever use of talc^b Includes borderline and invasive serous tumours

under 75 years of age who underwent surgery for ovarian cancer at one of two cancer hospitals in Athens between June 1989 and March 1991. The controls were 200 women under 75 years of age who were residents of Greater Athens and who visited patients hospitalized in the same wards as the cases during the study period. Ninety per cent of the eligible cases and 94% of the eligible controls agreed to participate. In-hospital interviews were conducted to collect information on a range of demographic, socioeconomic and reproductive factors, as well as information on exposure to hair dyes, analgesics, tranquilizers and talc. Exposure to talc was assessed qualitatively as ‘yes/no’ application of talc in the perineal region. In multivariable analyses, models were adjusted for age in 5-year groups, education, weight, age at menarche, menopausal status, age at menopause, parity, age at first birth, tobacco smoking status, alcohol use, coffee consumption and the other exposures of interest (use of analgesics, tranquilizers and hair dyes). Application of talc to the perineal region was reported by six cases [3.2%] and seven controls [3.5%] to yield an odds ratio of 1.1 (95% CI, 0.3–4.0) after adjustment for the potential confounders. [Limitations of this hospital-based case–control study included the very low prevalence of perineal use of talc.]

Purdie *et al.* (1995) conducted a case–control study among women in the three most populous Australian states—Queensland, New South Wales and Victoria. Cases were women, aged 18–79 years, who had been diagnosed with epithelial ovarian cancer between August 1990 and December 1993 at gynaecological oncology treatment centres in one of these three regions. Women were excluded if they had a metastatic tumour, were outside the eligible age range, could not be contacted, were too ill or were incapable of completing the questionnaire in conjunction with a trained interviewer (because of language difficulties or psychiatric conditions). Each case was confirmed by an independent pathological review of tissue specimens. Of 1116 cases identified during the study period, 201 (18%) were ineligible (e.g. due to a non-ovarian primary cancer or age at diagnosis). Among the 915 eligible cases, 824 (90%) agreed to participate and were interviewed. Reasons for non-participation included death before interview (50 cases), patient refusal (34 cases) and physician refusal (seven cases). Controls were identified from the electoral roll and were similar to the cases in age distribution and area of residence. Women were excluded as a control if they had a history of ovarian cancer or bilateral oophorectomy, could not be reached or could not complete the questionnaire. Among 1527 potential controls identified from the electoral roll, 1178 were located and found to be eligible (77%). Of these, 860 agreed to participate in the study (73% of the eligible controls). Reasons for ineligibility among the controls included failure to locate the individual (192), inability to complete the questionnaire due to language difficulties, a psychiatric condition, illness or death (105), previous bilateral oophorectomy (48) and age (four). Trained interviewers used a standardized questionnaire to collect information on medical, reproductive, family and occupational histories, as well as data on dietary factors and history of talc use. Questionnaires were administered face-to-face either in the clinic (for cases) or in the home of participant (for some cases and all controls). Covariates evaluated as potential confounders included parity, hysterectomy, tubal ligation, duration

of oral contraceptive use, age, education, body mass index, tobacco smoking status, family history of cancer and multiple menstrual and reproductive factors. Talc use around the abdomen or perineum was reported by 56.7% of cases and 52% of controls to yield an odds ratio of 1.3 (95% CI, 1.0–1.5) after adjustment for parity. Although enrolment in the electoral roll is mandatory in Australia, the authors determined that 28 cases [3.4%] had never enrolled and the enrolment status could not be confirmed for 46 cases [5.6%]. The results did not change when the analyses were limited to cases with confirmed enrolment in the electoral role.

Green *et al.* (1997) evaluated the association between tubal ligation or hysterectomy and the risk for ovarian cancer using the Australian study population described by Purdie *et al.* (1995). [The analysis by Green *et al.* (1997) used the same number of cases but five fewer controls than Purdie *et al.* (1995).] Duration of talc use was calculated as age at first reported use until age at occurrence of the earliest of any of the following events: surgical sterilization, reported last use of talc, diagnosis or interview. A modest increase in risk for ovarian cancer was observed with peritoneal use of talc (odds ratio, 1.3; 95% CI, 1.1–1.6). Neither duration of talc use nor age at first use were associated with risk for ovarian cancer, although the relative risks (95% CI) were not provided and the duration categories evaluated were not specified. When compared with women with no history of genital exposure to talc and patent fallopian tubes, women with a history of talc use and no history of surgical sterilization had the highest risk for ovarian cancer (odds ratio, 1.3; 95% CI, 1.0–1.7), while women with a history of tubal ligation or hysterectomy and no talc use had the lowest risk (odds ratio, 0.6; 95% CI, 0.5–0.8). [The primary limitation of this study was the restricted information on perineal use of talc.]

Shushan *et al.* (1996) examined the association between exposure to fertility drugs and the risk for ovarian cancer among 200 cases of epithelial ovarian cancer (164 invasive and 36 borderline) and 408 controls. All participants were living in Israel and were 36–64 years of age at enrolment into the study. Cases were identified through the Israel Cancer Registry from January 1990 to September 1993. Among 287 women who met the eligibility criteria (histologically confirmed diagnosis, cancer diagnosed and reported during study period, born between 1929 and 1957 and alive at time of interview), 87 (30.3%) were excluded because of inability to locate the patient or physician (25%), illness (1%), refusal by the physician (1%) or refusal by the patient (3%). Controls were identified by random-digit dialling and were matched to the cases by geographical area. Women were eligible to be included as a control if they were born in the same period as the cases. Potential controls were excluded if they had a history of bilateral oophorectomy (1%). Of 2072 telephone calls that successfully reached a household member, approximately half of the households [47.8%] contacted had a potentially eligible woman who was at home. Of these, 16.2% refused to participate and 10.7% were excluded because the woman did not speak Hebrew. Trained interviewers administered a standard questionnaire to all cases and controls. The questionnaire collected detailed information on reproductive history, use of oral contraceptives and fertility drugs, as well as exposure to talc (never/seldom, moderate/a lot). Although the main association of interest was use

of fertility drugs and the risk for ovarian cancer, the authors reported that 21 cases (10.5%) and 23 controls (5.6%) had a history of moderate or frequent use of talc, which yielded an unadjusted odds ratio of [1.97] ($P = 0.04$). [Limitations of this study included the very sparse information on talc use and the unavailability of adjusted results for the association between use of talc and the risk for ovarian cancer.]

Chang and Risch (1997) analysed the association between perineal use of powder and the risk for ovarian cancer among 450 cases and 564 population controls from metropolitan Toronto and southern Ontario, Canada. Cases were diagnosed between November 1989 and October 1992 and were between the ages of 35 and 79 years at entry into the study. Of 631 cases identified during the study period, 71.3% (450) were interviewed and included in the analysis. Reasons for non-participation included death (8.7%), physician refusal (4.6%), severe illness (4.8%), loss to follow-up (2.7%) and patient refusal (7.9%). Potential controls were identified through records of the Ontario Ministry of Finance based on their residence and age, were matched to cases within 15-year age groups and were excluded from the study if they had a history of bilateral oophorectomy more than 1 year before entry into the study. Among 873 eligible controls identified, 309 [35.4%] did not participate. Reasons included participant refusal (30.2%), illness (1.9%) or loss to follow-up (3.2%). Interviewers administered a standard questionnaire during an in-home interview to obtain information on the history, frequency and duration of use of talcum and cornstarch powder, as well as multiple medical and reproductive covariates of interest. Talc exposure was categorized on the basis of 'any' exposure in the perineal area, on the method of application (directly to the perineum after bathing or showering, dusting on sanitary napkins), on the frequency of application (< 10, 10–25, > 25 applications per month) and on the duration of exposure (< 30, 30–40, > 40 years of use). Multiple logistic regression was used in the analyses, with adjustment for age, duration of oral contraceptive use, parity (defined as the number of full-term pregnancies), duration of lactation for each pregnancy, history of tubal ligation or hysterectomy and family history of breast or ovarian cancer. Forty-four per cent of cases and 36% of controls reported 'any' talc use in the perineal area to yield an odds ratio of 1.4 (95% CI, 1.1–1.9). Among the specific types of talc exposure, application to the perineum after bathing was associated with a borderline significant increase in risk (odds ratio, 1.3; 95% CI, 1.0–1.7), while application on sanitary napkins (a less common use in this study population) was associated with an elevated but non-significant increase in risk (odds ratio, 1.3; 95% CI, 0.9–2.0). A borderline significant trend was seen with increasing duration of exposure to talc (odds ratio per 10 years of exposure, 1.1; 95% CI, 1.0–1.2), but not with increasing frequency of exposure. An analysis of duration by category (< 30, 30–40, > 40 years) did not suggest a dose-response relationship (odds ratios of 1.0; 1.7; 95% CI, 1.1–2.6; 1.4; 95% CI, 1.0–2.2 and 0.9; 95% CI, 0.5–1.4, respectively). Use of cornstarch in the perineal area, either alone or in conjunction with occasional talc, was not associated with the risk for ovarian cancer, although prevalence of use was low (less than 2% of subjects). To evaluate exposure pre- and post-1970, as well as exposure pre- and post-tubal ligation or hysterectomy, the authors assumed that participants initiated

perineal use of after-bath talc at the age of 20 years. A similar, non-significantly elevated, risk for ovarian cancer was seen for use pre- and post-1970. A higher odds ratio was seen for use of after-bath talc before tubal ligation or hysterectomy (odds ratio, 1.1; 95% CI, 1.0–1.2) than for use after these surgical procedures (odds ratio, 1.0; 95% CI, 0.8–1.3). These estimates did not change when different starting ages, between 15 and 24 years, were used in the analysis. The authors also evaluated the association between perineal use of talc and invasive and borderline cancers separately, and found that the risk was elevated for both tumour types but was significant only for invasive tumours. In addition, risk was similar across the major histological subtypes of ovarian cancer (serous, mucinous, endometrioid) (see Table 2.4). [Limitations of this study included the lack of information on use of talc.]

Cook *et al.* (1997) evaluated the association between use of genital powders or deodorants and the risk for ovarian cancer in a case–control study conducted in three counties of western Washington State, USA. Cases were aged 20–79 years at diagnosis, were diagnosed with borderline or invasive epithelial ovarian cancer between 1986 and 1988 and were identified using the population-based Cancer Surveillance System of western Washington. Controls were identified using random-digit dialling, were residents of the three counties of interest and were similar in age to the cases. Among 512 eligible cases identified, 329 were interviewed (64.3%) and 313 were included in the analysis [61.1%]. A total of 183 eligible cases were not interviewed due to death (104), physician or patient refusal (73) or loss to follow-up (six). An additional 16 cases who were interviewed were excluded from the analysis because of non-white race (seven) and unknown genital use of powder (nine). Among 721 women identified as potential controls, 521 were interviewed (72.3%) and 422 were included in the analysis [58.5%]. Reasons for excluding interviewed controls from the analysis included: non-white race (28), age greater than 79 years (five), history of bilateral oophorectomy (58), unknown oophorectomy status (four) and unknown genital use of powder (four). Information on powder use, including the type, method, frequency and duration of use, and the covariates of interest was collected during in-person interviews. Covariates considered to be potential confounders in multivariable analyses included age, education, income, marital status, body mass index, oral contraceptive use and parity. A history of ‘any’ lifetime genital powder use (perineal dusting, diaphragm storage, use on sanitary napkins or use of deodorant spray) was reported by 50.8% of cases and 39.3% of controls to yield an odds ratio of 1.5 (95% CI, 1.1–2.0) after adjustment for age. Among the individual methods of genital use of powder, risk was significantly elevated only for exclusive perineal dusting (odds ratio, 1.8; 95% CI, 1.2–2.9) after adjustment for age. In analyses adjusted for age and other types of genital use of powder, both perineal dusting (odds ratio, 1.6; 95% CI, 1.1–2.3) and genital deodorant spray (odds ratio, 1.9; 95% CI, 1.1–3.1) were associated with risk for ovarian cancer, while use of powder on a diaphragm or on sanitary napkins was not associated with an increased risk. There was no evidence of an increasing trend in risk with greater duration of perineal dusting, but a significant positive trend was noted for both duration (odds ratio, 2.7; 95% CI, 1.1–6.6 for > 12 cumulative lifetime months; *p* for

trend < 0.05) and number of lifetime applications (odds ratio, 2.6; 95% CI, 0.9–7.6 for > 500 lifetime applications; p for trend < 0.05) of genital deodorant spray. The effect estimates did not change materially when perineal use of dusting powder after the date of tubal ligation or hysterectomy was excluded. Risk was significantly elevated among women with any history of perineal dusting before 1976 (odds ratio, 1.8; 95% CI, 1.1–2.9), but the authors were unable to evaluate risk for use exclusively after 1976 due to the small number of women (four cases and 10 controls) who had had this exposure. Among the individual types of powder evaluated (cornstarch, talcum powder, baby powder, deodorant powder, scented body/bath powder), risk for ovarian cancer was non-significantly elevated for ‘any’ use of talcum powder (odds ratio, 1.6; 95% CI, 0.9–2.8) and bath/body powder use (odds ratio, 1.5; 95% CI, 0.9–2.4) after adjustment for age and other types of powder use (yes/no). The authors also evaluated the association between any genital use of powder and the risk for the major histological subtypes of ovarian cancer (see Table 2.4). Risk was significantly elevated for serous tumours (odds ratio, 1.7; 95% CI, 1.1–2.5) and all other tumour types (odds ratio, 1.8; 95% CI, 1.1–2.8) but not for mucinous or endometrioid tumours. [Limitations of this study included the relatively low participation rates among the cases and controls.]

Eltabbakh *et al.* (1998) compared risk factors among 50 cases of primary extra-ovarian peritoneal carcinoma (the ‘study’ group) and 503 cases of primary epithelial ovarian cancer (the ‘control’ group) treated at Roswell Park Cancer Institute in Buffalo, NY (USA), between October 1982 and October 1996. No healthy controls were enrolled in this study. Diagnoses were reviewed by staff in the Division of Pathology (study and control groups) and were confirmed by a single pathologist as part of another study (study group only). Information on reproductive history, menstrual history, use of hormones and contraceptives and personal hygiene was collected through a self-administered, 44-item questionnaire which all patients were asked to complete during the hospital admission process. All women who returned a questionnaire were eligible to be included in the study. Among these patients, the overall questionnaire response rate was 60%. Response was inversely correlated with severity of disease and response rates were similar for the two diagnoses included in this study. Because data on perineal talc use was missing for 37 patients in the ‘control’ group, only 466 ovarian cancer patients were included in the analysis. Women who had primary ovarian cancer were significantly more likely to report a history of perineal use of talc compared with women who had primary peritoneal cancer (48.1% versus 26.0%; [crude odds ratio = 2.6] $P = 0.003$). Among the other characteristics examined, only age and age at menarche differed significantly in the two groups. [Limitations of this study included the minimal information on talc use, the low questionnaire response rate among study participants, particularly among the patients with more advanced disease, the use of a self-administered questionnaire completed during the admissions process, which may have limited the quality of the responses, and the lack of a ‘healthy’ comparison group.]

Godard *et al.* (1998) evaluated risk factors for familial and sporadic ovarian cancer in a population of French Canadian women in Montréal, Quebec (Canada). Of 231 cases

who were identified between 1995 and 1996 at two gynaecological oncology clinics in Montréal, 183 (79.2%) were interviewed and 170 (73.6%) were included in the analysis. Reasons for non-inclusion were death ($n = 21$), refusal/unavailability to participate ($n = 12$), loss to follow-up ($n = 15$) and tumours were non-epithelial in origin ($n = 13$). All cases were between the ages of 20 and 84 years at diagnosis, with a mean age at diagnosis of 53.7 years and a mean age at interview of 55.9 years. Controls were identified using a modified random-digit dialling method and were frequency-matched to cases by age (within 1 year) and French Canadian ethnicity. The mean age at interview for the controls was 56.7 years. Among 750 households contacted regarding participation in the study, 66.7% ($n = 500$) either did not have an eligible female resident or did not reply to the researchers' inquiries and 10.7% refused to participate. A total of 170 women were interviewed and included in the analysis as controls. A standardized 57-item questionnaire was used to obtain information on the family, medical and reproductive history of each participant. Cases were interviewed either by telephone (30%) or in the study clinics (70%). No information was given on the methods of interview for control subjects. Information on family history of cancer was collected to determine whether risk factors differed for the sporadic and familial cases of ovarian cancer. Familial cases were those patients who had one or more family members (first, second or third degree relatives) with breast cancer diagnosed before 55 years of age or ovarian cancer diagnosed at any age. Sporadic cases were those patients who had no family members with breast cancer diagnosed before 55 years of age or with ovarian cancer diagnosed at any age. Perineal exposure to talc was assessed qualitatively (ever/never, with 'never' as the baseline). Covariates that were considered to be potential confounding variables were age at menarche, age at menopause, parity, age at first and last childbirth, duration of oral contraceptive use, age at last oral contraceptive use, tubal ligation, alcohol use and previous breast or abdominal surgery. Talc exposure was more common in cases than controls, with 10.6% of the cases and 4.7% of the controls reported perineal use of talc ($P = 0.06$). No difference between perineal use of talc was reported in the familial and sporadic cases ($P = 0.79$). Multivariate analyses were performed comparing all cases, (all, sporadic, familial) with controls. In these analyses, perineal use of talc was associated with a non-significant increase in the total risk for ovarian cancer (odds ratio, 2.5; 95% CI, 0.9–6.6; $P = 0.07$). Risk was similarly non-significantly elevated for sporadic (odds ratio, 2.5; 95% CI, 0.9–7.1) and familial cases (odds ratio, 3.3; 95% CI, 0.9–12.4) compared with the controls. [Limitations of this study included its small size and the lack of any detailed information on perineal use of talc. The control participation rates may have been low (although this is not clear) and it is not certain how representative the controls were.]

Cramer *et al.* (1999) analysed the association between genital exposure to talc and the risk for primary epithelial ovarian cancer among 563 cases and 523 controls residing in eastern Massachusetts and New Hampshire, USA. Cases were identified between May 1992 and March 1997 through hospital tumour boards or statewide cancer registries. Among 1080 cases diagnosed in this period (including borderline tumours), 203 (18.8%)

were excluded due to death, change of address, inability to speak English, no telephone in residence or a non-ovarian primary cancer. Of the 877 eligible cases remaining after these exclusions, 563 (64%) were included in the analysis. The remaining 314 cases were excluded because of physician refusal ($n = 126$) and patient refusal ($n = 136$). Pathology reports were reviewed to confirm the diagnoses for all cases, and slides were requested and reviewed in the case of discrepancies between the reported histology and the histology assigned based on the pathology report review. Controls were identified by random-digit dialling and town resident books (to identify additional women over the age of 60 years who lived in Massachusetts) and were frequency-matched to cases by age (within 4 years) and location of residence. Of the potentially eligible controls, 72% of those identified by random-digit dialling and 49% of those identified through town books agreed to participate. All study participants were interviewed in-person using a standardized questionnaire to obtain information on their medical and reproductive histories, family history and personal habits. The questionnaire also asked multiple questions on powder use, including route of exposure (application to non-genital areas, application to perineum, sanitary napkins or underwear, husband's use of powders in his genital area), brand of powder used (talc, cornstarch), age at first use, duration and frequency of use (< 30 , $30-39$, > 40 uses per month). Participants were asked about exposures that occurred at least 1 year before the date of diagnosis (cases) or the date of interview (controls). The results were adjusted for the following potential confounding variables: age, state of residence, body mass index, parity, oral contraceptive use, family history of breast or ovarian cancer and history of tubal ligation. The prevalence of talc use was higher among cases than controls; 44.6% of cases and 36.1% of controls reported 'any' use of talc (included use in both genital and non-genital areas) and 27.0% of cases and 18.2% of controls reported 'genital' use of talc (included dusting of perineum/sanitary napkins/underwear, either exclusively or in combination). Talc use in non-genital areas was not associated with risk when compared with women who did not use personal powder (odds ratio, 1.1; 95% CI, 0.8–1.5). However, genital use of talc was associated with a significant 60% increase in risk (odds ratio, 1.6; 95% CI, 1.2–2.2). Women who reported more than one method of talc use in the genital area had an even greater risk for ovarian cancer (odds ratio, 2.2; 95% CI, 1.3–3.6). No association was observed between genital use of talc and risk for ovarian cancer among women who had undergone tubal ligation after adjustment for age (odds ratio, 1.0; 95% CI, 0.5–2.1). Because of the low prevalence of use ($< 1\%$ of the study population) of cornstarch, evaluation of this product was uninformative. When women who had been exposed to powder only in non-genital areas were excluded from the analysis, no linear trend was observed between risk for ovarian cancer and age at first genital use of talc, duration of use, frequency of use or total number of lifetime applications. However, when non-genitally exposed women were included in the analysis, a significant linear trend was observed with increasing number of lifetime applications, after talc applications that occurred during non-ovulatory years or after tubal ligation or hysterectomy were excluded ($P = 0.02$). Additional findings of interest included: a non-significant increase in risk among married women with no

personal talc use whose husbands had used talc for genital hygiene (odds ratio, 1.5; 95% CI, 0.9–2.5); and a stronger association between genital use of talc and risk for ovarian cancer among women who had used talc before their first live birth (odds ratio, 1.6; 95% CI, 1.1–2.3) than for women who had used it exclusively after their first live birth (odds ratio, 1.0; 95% CI, 0.4–2.5). The association with genital use of talc was strongest for serous invasive tumours (odds ratio, 1.7; 95% CI, 1.2–2.4). No association was observed for endometrioid/clear-cell (odds ratio, 1.0; 95% CI, 0.7–1.6) or mucinous tumours (odds ratio, 0.79; 95% CI, 0.4–1.4) (see Table 2.4).

Wong *et al.* (1999) reported the results of a case–control study conducted at Roswell Park Cancer Institute, Buffalo, NY (USA) of 499 cases treated between October 1982 and October 1992 (largely those reported by Eltabbakh *et al.*, 1998) and 755 hospital-based controls. The controls were randomly selected from a registry of patients who were being treated for non-gynaecological malignancies and were frequency-matched to cases by age at diagnosis (within 5 years). The most common diagnoses among controls were colorectal (43.3%) and skin cancers (34.5%) and leukaemia (17.7%). All participants completed the self-administered, 44-item questionnaire that all patients were asked to complete during the hospital admission process. All analyses were adjusted for age at diagnosis, parity, oral contraceptive use, tobacco smoking, family history of ovarian cancer, age at menarche, menopausal status, income, education, geographical location and history of tubal ligation or hysterectomy. The analysis was restricted to 462 cases and 693 controls with information on perineal use of talc. ‘Ever’ use of talc (genital or non-genital) was reported by 47.8% of the cases and 44.9% of the controls, while use of talc in the genital or thigh area was reported by 34.0% of the cases and 32.2% of the controls. There was no association between any method of talc use and the risk for ovarian cancer after adjusting for several potentially confounding variables. The adjusted odds ratio for talc use in the genital or thigh area was 1.0 (95% CI, 0.8–1.3). Duration of talc use was similar in the cases and controls, and no association between talc use and the risk for ovarian cancer was found for any duration category. No significant association was observed between talc use and any of the major histological subtypes of ovarian cancer (see Table 2.4); the odds ratio for serous cystadenocarcinoma was 1.2 (95% CI, 0.7–2.1). No evidence was found of effect modification by history of tubal ligation or hysterectomy. Among women who had not undergone tubal ligation or hysterectomy, the odds ratio for the association between talc use and risk for ovarian cancer was 1.2 (95% CI, 0.8–1.6) while among women who had undergone tubal ligation or hysterectomy, the odds ratio was 0.8 (95% CI, 0.5–1.2). [Limitations of the study included the sparse information on talc use. In addition, the use of hospital controls with non-gynaecological malignancies may have caused selection bias. As noted in the earlier report by Eltabbakh *et al.* (1998), the response rate to the questionnaire was low in this study population, particularly among the patients with more advanced disease.]

Ness *et al.* (2000) examined whether factors related to an inflammatory response of the ovarian epithelium (such as exposure to talc, endometriosis, cysts and hyperthyroidism) played a role in the risk for ovarian cancer. The study was conducted

among 767 recently diagnosed cases of epithelial ovarian cancer and 1367 population-based controls. Cases were aged 20–69 years and were identified between 1994 and 1998 at 39 hospitals in the Delaware Valley region (USA). Of 1253 potentially eligible cases, 61.2% were interviewed and included in the analysis. Reasons for excluding women from the study included: diagnosis more than 6 months before the interview ($n = 296$), severe illness or death ($n = 69$), unavailability of contact information ($n = 15$), physician refusal ($n = 14$) or patient refusal ($n = 92$). Controls were identified through random-digit dialling (for controls ≤ 65 years of age) and Health Care Financing Administration lists (for controls 65–69 years of age) and were frequency-matched to cases by age and location of residence. Overall, 72% of the eligible potential controls agreed to participate in the study. A pathological review was conducted for a subset of the cases ($n = 120$). When compared with the original diagnosis, the central review was 95% concordant for invasiveness and 82% concordant for cell type. The original pathological diagnosis was used in the analysis for all cases. A standardized, 1.5-hour interview was conducted in the homes of the participants to collect information on menstrual and reproductive history, sexual activity, use of contraceptives, history and duration of talc use (genital and non-genital applications and exposure via male sexual partners). Talc use was categorized according to the method of application (never, feet, genital/rectal, sanitary napkins, underwear, diaphragm or cervical cap, or male partner) and duration of exposure (< 1 year, 1–4 years, 5–9 years, > 10 years). Unconditional logistic regression adjusted for age, parity, race, family history of ovarian cancer, oral contraceptive use, tubal ligation, hysterectomy and lactation was used in all analyses. A history of talc use in the genital/rectal area was reported by 161 cases [21.0%] and 219 controls [16.0%] to yield an adjusted odds ratio of 1.5 (95% CI, 1.1–2.0). Significant associations were also observed for the use of talc on sanitary napkins (odds ratio, 1.6; 95% CI, 1.1–2.3) and on underwear (odds ratio, 1.7; 95% CI, 1.2–2.4). The use of talc on the feet, arms or breasts was associated with a significant 40% increase in risk; however, women may also have used talc on more than one area of the body, including the genital and/or rectal area. Use of talc on diaphragms or cervical caps and use by a male sexual partner were not associated with the risk for ovarian cancer. There was no clear trend between risk for ovarian cancer and increasing duration of use of talc on the genital and/or rectal area or feet. Adjusted odds ratios of 2.0 (95% CI, 1.0–4.0), 1.6 (95% CI, 1.1–2.3), 1.2 (95% CI, 0.8–1.9) and 1.2 (95% CI, 1.0–1.5) were observed for < 1 year, 1–4 years, 5–9 years and ≥ 10 years of use, respectively. [Limitations of this analysis included the sparse information on talc use. In analyses of duration, the use of talc on the feet was also included as an exposure. The relatively low participation rates among cases was also a limitation of the study.]

Langseth and Kjaerheim (2004) (described in detail in Section 2.1.2(b)) evaluated the association between employment in the pulp and paper industry in Norway and the risk for ovarian cancer. In addition to the assessment of occupational exposure, information was collected on hygienic use of talc and potential confounders for a subset of the cases and controls during a personal interview conducted at the mills or by telephone. Exposure to hygienic talc products was categorized as ever/never for personal use on diapers,

sanitary napkins, underwear or husband's use in the genital area. Thirty-five cases and 102 of the eligible controls or their next of kin agreed to an interview and an additional 19 women who were not cases were interviewed and included in secondary analyses as supplementary controls. A family member completed the interview (due to the death of the case or control) for 25 of the cases and 31 of the controls. Use of talc on the genital area was reported by 12 cases and 53 controls to yield an odds ratio of 1.2 (95% CI, 0.4–3.2). [The primary limitations of this analysis were the small number of cases, the small percentage of cases and controls who were interviewed to obtain information on the covariates of interest and use of surrogate respondents to obtain information on covariates for the deceased cases and controls. The Working Group noted that hygienic exposure to talc was assessed retrospectively in the nested case–control study.]

Mills *et al.* (2004) evaluated the association between perineal exposure to talc and the risk for ovarian cancer in an ethnically diverse population from 22 counties of central California, USA. The study included 256 incident cases diagnosed between 1 January 2000 and 31 December 2001 and identified through two regional cancer registries using rapid case ascertainment procedures and 1122 controls identified by random-digit dialling. Controls were frequency-matched to the cases by age and ethnicity. Pathology reports were reviewed centrally for a subset of the cases to confirm the diagnosis, subtype and invasiveness of each cancer. Potential controls were ineligible for inclusion in the study if they were under 18 years of age, were not a resident of the counties of interest or if they had a history of epithelial ovarian cancer or bilateral oophorectomy. Among 652 cases identified during the study period, 263 (40.3%) were excluded due to: language or hearing difficulties ($n = 17$), death ($n = 76$), physician refusal ($n = 10$), severe illness ($n = 41$) or unavailability of current contact information ($n = 119$). Of the 389 eligible cases who were contacted regarding participation in the study, 256 (65.8%) agreed to participate and were interviewed. Of a total of 2327 potential controls, 740 (31.8%) were excluded from the study due to: age ($n = 80$), location of residence ($n = 21$), language difficulties ($n = 10$), previous bilateral oophorectomy ($n = 252$), severe illness ($n = 19$) or change of address or telephone number or inability to contact the woman after repeated attempts ($n = 358$). Of the 1587 potential controls who were contacted and found to be eligible, 1122 (70.7%) agreed to participate and were interviewed. All cases and controls were interviewed by telephone to obtain information on their medical history, covariates of interest and history of perineal exposure to talc, including the frequency, duration and calendar years of use. Information on talc use was unavailable for seven cases and 17 controls; thus, the final study population for this analysis included 249 cases and 1105 controls. For the final models, unconditional logistic regression adjusted for age, race/ethnicity, duration of oral contraceptive use and breastfeeding was used. Additional covariates considered to be potential confounders included family history of breast cancer or ovarian cancer, parity, history of pregnancy, body mass index, hysterectomy, tubal ligation and duration of postmenopausal use of hormones. A history of perineal talc use was reported by 42.6% of the cases and 37.1% of the controls to yield an adjusted odds ratio of 1.4 (95% CI, 1.0–1.9). A significant trend ($P = 0.015$) with increasing frequency

of talc use was observed. The greatest risk for ovarian cancer was observed among women with the highest frequency of use (odds ratio, 1.7 for use 4–7 times per week; 95% CI, 1.1–2.6). There was a borderline significant trend with increasing duration of use ($P = 0.045$). The highest risk was observed among women with 4–12 years of use (odds ratio, 1.9; 95% CI, 1.2–3.0) and elevated but non-significant risks were seen among women with longer durations of use with odds ratios of 1.5 (95% CI, 0.9–2.3) and 1.2 (95% CI, 0.7–2.1) for 13–30 and > 30 years of use, respectively. A borderline significant trend was noted for cumulative talc use (frequency times duration of use), although this was also not clear-cut ($P = 0.051$). The highest risks were observed in the second and third quartiles of cumulative talc use. When examined according to the time of use, the risk was higher among women who had first used talc after 1975 (odds ratio, 1.9; 95% CI, 1.3–2.9) than among those who had first used talc before or during 1975 (odds ratio, 1.2; 95% CI, 0.8–1.8). Risk was also higher among women who were aged 20 years or more at first talc use than among those who were under 20 years of age and among women who initiated talc use after their first birth than among those who had some use before their first birth. When time since last use was examined, women who had last used talc 1–2 years previously had the highest risk (odds ratio, 2.4; 95% CI, 1.4–4.1); women who had last used it 3–20 years previously had an elevated but non-significant risk for ovarian cancer (odds ratio, 1.6; 95% CI, 0.9–2.7). Modification of the association between perineal use of talc and risk for ovarian cancer by tubal ligation, hysterectomy, parity, oral contraceptive use, postmenopausal use of hormones and body mass index was also evaluated. Risk was higher among women who had not had tubal ligation (odds ratio, 1.5; 95% CI, 1.1–2.2) than among those who had (odds ratio, 0.9; 95% CI, 0.5–1.7), although the interaction was not statistically significant. Risk was also higher among women who had ever been pregnant (odds ratio, 1.4; 95% CI, 1.1–2.0) than among those who had never been pregnant (odds ratio, 0.9; 95% CI, 0.4–2.3) and among women who had no history of oral contraceptive use (odds ratio, 1.6; 95% CI, 1.0–2.6) than among those who had used oral contraceptives (odds ratio, 1.3; 95% CI, 0.9–1.8). No evidence was found of a modification of effect by hysterectomy status, body mass index or postmenopausal use of hormones. [Limitations of this study included the low participation rate and relatively small number of cases. In addition, pathology was not confirmed for all cases, which may have resulted in some misclassification of histological subtype.]

2.3 Use of talc in pleurodesis

The use of talc or iodized talc to produce pleurodesis began in the 1930s as a treatment for recurrent spontaneous pneumothorax or pleural effusions. The therapy involves the introduction of 0.5–10 g talc directly into the pleura using intrapleural injection. In recent decades, the therapy has most commonly been restricted to use for the treatment of malignant pleural effusions.

An individual case report described a lung adenocarcinoma that was diagnosed 2 years after pleurodesis with iodized talc (Jackson & Bennett, 1973).

A survey was reported (Research Committee of the British Thoracic Association and the Medical Research Council Pneumoconiosis Unit, 1979) of the long-term effects of pleurodesis with talc and kaolin among a series of British patients who were followed for 14–40 years. The one talc mentioned (BP Indian Finex) was reported not to contain fibrous amphiboles, but it was unclear if that was true of all the talcs used. Three lung cancers were observed (2.14 expected, $P > 0.3$) among 210 talc pleurodesis patients. Two of the lung cancer patients developed tumours on the opposite side from where treatment had occurred (18-month and 19-year intervals between treatment and death). The third patient had an oat cell carcinoma (site unknown) and died 32 years after treatment. No cases of mesothelioma were reported.

Viskum *et al.* (1989) reported on 99 Danish patients who had been treated in 1954–64 by pleurodesis with talc at doses that ranged from 0.5 to 4.9 g and who were followed for at least 20 years. Three deaths from lung cancer occurred [expected number of cases not provided], one on the side opposite from where treatment had occurred and two with no origin reported. No cases of mesothelioma were reported. [The Working Group noted that these reports are difficult to interpret because of the high prevalence of lung disease in the patient groups, which could be related to risk factors such as tobacco smoking. The type or source of talc used was not clear, although it was assumed to be pharmaceutical grade. No case of mesothelioma was observed but the number of expected cases would probably be very low.]

2.4 References

- Blum S, Arp EW Jr, Smith AH, Tyroler HA (1979). Stomach cancer among rubber workers: an epidemiologic investigation. In: Lemen, R., Dement, JM, eds. *Dusts and Disease, Proceedings of the Conference on Occupational Exposures to Fibrous and Particulate Dust and Their Extension into the Environment*. Park Forest South, IL, Pathotox Publisher, Inc., pp. 325–334.
- Booth M, Beral V, Smith P (1989). Risk factors for ovarian cancer: a case–control study. *Br J Cancer*, 60:592–598. PMID:2679848
- Chang S, Risch HA (1997). Perineal talc exposure and risk of ovarian carcinoma. *Cancer*, 79:2396–2401. doi:10.1002/(SICI)1097-0142(19970615)79:12<2396::AID-CNCR15>3.0.CO;2-M. PMID:9191529
- Chen Y, Wu P-C, Lang J-H *et al.* (1992). Risk factors for epithelial ovarian cancer in Beijing, China. *Int J Epidemiol*, 21:23–29. doi:10.1093/ije/21.1.23. PMID:1544753
- Coggiola M, Bosio D, Pira E *et al.* (2003). An update of a mortality study of talc miners and millers in Italy. *Am J Ind Med*, 44:63–69. doi:10.1002/ajim.10240. PMID:12822137
- Cook LS, Kamb ML, Weiss NS (1997). Perineal powder exposure and the risk of ovarian cancer. *Am J Epidemiol*, 145:459–465. PMID:9048520
- Cramer DW, Liberman RF, Titus-Ernstoff L *et al.* (1999). Genital talc exposure and risk of ovarian cancer. *Int J Cancer*, 81:351–356. doi:10.1002/(SICI)1097-0215(19990505)81:3<351::AID-IJC7>3.0.CO;2-M. PMID:10209948

- Cramer DW, Welch WR, Scully RE, Wojciechowski CA (1982). Ovarian cancer and talc: a case-control study. *Cancer*, 50:372–376. doi:10.1002/1097-0142(19820715)50:2<372::AID-CNCR2820500235>3.0.CO;2-S. PMID:7083145
- Eltabbakh GH, Piver MS, Natarajan N, Mettlin CJ (1998). Epidemiologic differences between women with extraovarian primary peritoneal carcinoma and women with epithelial ovarian cancer. *Obstet Gynecol*, 91:254–259. doi:10.1016/S0029-7844(97)00650-9. PMID:9469285
- Gertig DM, Hunter DJ, Cramer DW *et al.* (2000). Prospective study of talc use and ovarian cancer. *J Natl Cancer Inst*, 92:249–252. doi:10.1093/jnci/92.3.249. PMID:10655442
- Godard B, Foulkes WD, Provencher D *et al.* (1998). Risk factors for familial and sporadic ovarian cancer among French Canadians: a case-control study. *Am J Obstet Gynecol*, 179:403–410. doi:10.1016/S0002-9378(98)70372-2. PMID:9731846
- Green A, Purdie D, Bain C *et al.*; Survey of Women’s Health Study Group (1997). Tubal sterilisation, hysterectomy and decreased risk of ovarian cancer. *Int J Cancer*, 71:948–951. doi:10.1002/(SICI)1097-0215(19970611)71:6<948::AID-IJC6>3.0.CO;2-Y. PMID:9185694
- Harlow BL, Cramer DW, Bell DA, Welch WR (1992). Perineal exposure to talc and ovarian cancer risk. *Obstet Gynecol*, 80:19–26. PMID:1603491
- Harlow BL, Weiss NS (1989). A case-control study of borderline ovarian tumors: the influence of perineal exposure to talc. *Am J Epidemiol*, 130:390–394. PMID:2750733
- Hartge P, Hoover R, Leshner LP, McGowan L (1983). Talc and ovarian cancer. *JAMA*, 250:1844. doi:10.1001/jama.250.14.1844. PMID:6620481
- Hartge P, Stewart P (1994). Occupation and ovarian cancer: a case-control study in the Washington, DC, metropolitan area, 1978–1981. *J Occup Med*, 36:924–927. PMID:7807277
- Jackson JW, Bennett MH (1973). Chest wall tumour following iodized talc pleurodesis. *Thorax*, 28:788–793. doi:10.1136/thx.28.6.788. PMID:4787992
- Katsnelson BA, Mokronosova KA (1979). Non-fibrous mineral dusts and malignant tumors: an epidemiological study of mortality. *J Occup Med*, 21:15–20. PMID:215733
- Langseth H, Andersen A (1999). Cancer incidence among women in the Norwegian pulp and paper industry. *Am J Ind Med*, 36:108–113. doi:10.1002/(SICI)1097-0274(199907)36:1<108::AID-AJIM15>3.0.CO;2-N. PMID:10361594
- Langseth H, Kjaerheim K (2004). Ovarian cancer and occupational exposure among pulp and paper employees in Norway. *Scand J Work Environ Health*, 30:356–361. PMID:15529799
- Leophonte P, Basset MF, Pincemin J *et al.* (1983). [Mortality of talc workers in France: a retrospective epidemiological study.] *Rev Fr Mal Respir*, 11:489–490.
- Leophonte P, Didier A (1990) French talc pneumoconiosis. In: Bignon, J., ed., *Health Effects of Phyllosilicates*, Berlin Heidelberg, Springer-Verlag, pp. 203–209.
- Mills PK, Riordan DG, Cress RD, Young HA (2004). Perineal talc exposure and epithelial ovarian cancer risk in the Central Valley of California. *Int J Cancer*, 112:458–464. doi:10.1002/ijc.20434. PMID:15382072
- Ness RB, Grisso JA, Cottreau C *et al.* (2000). Factors related to inflammation of the ovarian epithelium and risk of ovarian cancer. *Epidemiology*, 11:111–117. doi:10.1097/00001648-200003000-00006. PMID:11021606
- Purdie D, Green A, Bain C *et al.*; Survey of Women’s Health Study Group (1995). Reproductive and other factors and risk of epithelial ovarian cancer: an Australian case-control study. *Int J Cancer*, 62:678–684. doi:10.1002/ijc.2910620606. PMID:7558414

- Research Committee of the British Thoracic Association and the Medical Research Council Pneumoconiosis Unit; Research Council Pneumoconiosis U (1979). A survey of the long-term effects of talc and kaolin pleurodesis. *Br J Dis Chest*, 73:285–288. doi:10.1016/0007-0971(79)90054-8. PMID:553661
- Rosenblatt KA, Szklo M, Rosenshein NB (1992). Mineral fiber exposure and the development of ovarian cancer. *Gynecol Oncol*, 45:20–25. doi:10.1016/0090-8258(92)90485-2. PMID:1601331
- Rubino GF, Scansetti G, Piolatto G (1979) Mortality and morbidity among talc miners and millers in Italy. In: Lemen, R., Dement, J.M., eds. *Dusts and Disease, Proceedings of the Conference on Occupational Exposures to Fibrous and Particulate Dust and Their Extension into the Environment*. Park Forest South, IL: Pathotox Publisher, Inc.,pp. 357–363.
- Rubino GF, Scansetti G, Piolatto G, Romano CA (1976). Mortality study of talc miners and millers. *J Occup Med*, 18:187–193. doi:10.1097/00043764-197603000-00013. PMID:1255280
- Selevan SG, Dement JM, Wagoner JK, Froines JR (1979). Mortality patterns among miners and millers of non-asbestiform talc: preliminary report. *J Environ Pathol Toxicol*, 2:273–284. PMID:512559
- Shushan A, Paltiel O, Iscovich J *et al.* (1996). Human menopausal gonadotropin and the risk of epithelial ovarian cancer. *Fertil Steril*, 65:13–18. PMID:8557128
- Siemiatycki J, editor (1991). *Risk Factors for Cancer in the Workplace*. Boca Raton, FL: CRC Press
- Straif K, Chambless L, Weiland SK *et al.* (1999). Occupational risk factors for mortality from stomach and lung cancer among rubber workers: an analysis using internal controls and refined exposure assessment. *Int J Epidemiol*, 28:1037–1043. doi:10.1093/ije/28.6.1037. PMID:10661645
- Straif K, Keil U, Taeger D *et al.* (2000). Exposure to nitrosamines, carbon black, asbestos, and talc and mortality from stomach, lung, and laryngeal cancer in a cohort of rubber workers. *Am J Epidemiol*, 152:297–306. doi:10.1093/aje/152.4.297. PMID:10968374
- Thomas TL, Stewart PA (1987). Mortality from lung cancer and respiratory disease among pottery workers exposed to silica and talc. *Am J Epidemiol*, 125:35–43. PMID:3024482
- Tzonou A, Polychronopoulou A, Hsieh C-C *et al.* (1993). Hair dyes, analgesics, tranquilizers and perineal talc application as risk factors for ovarian cancer. *Int J Cancer*, 55:408–410. doi:10.1002/ijc.2910550313. PMID:8375924
- Viskum K, Lange P, Mortensen J (1989). Long term sequelae after talc pleurodesis for spontaneous pneumothorax. *Pneumologie*, 43:105–106. PMID:2717548
- Wergeland E, Andersen A, Baerheim A (1990). Morbidity and mortality in talc-exposed workers. *Am J Ind Med*, 17:505–513. doi:10.1002/ajim.4700170408. PMID:2327417
- Whittemore AS, Wu ML, Paffenbarger RS Jr *et al.* (1988). Personal and environmental characteristics related to epithelial ovarian cancer. II. Exposures to talcum powder, tobacco, alcohol, and coffee. *Am J Epidemiol*, 128:1228–1240. PMID:3195564
- Wild, P. (2000) [An epidemiological mortality study in the Talc-producing industry: Study Report] (INRS/EE Report TMT), Paris, Institut National de la Recherche Scientifique (in French)
- Wild P (2006). Lung cancer risk and talc not containing asbestiform fibres: a review of the epidemiological evidence. *Occup Environ Med*, 63:4–9. doi:10.1136/oem.2005.020750. PMID:16361399

- Wild P, Leodolter K, Réfrégier M *et al.* (2002). A cohort mortality and nested case-control study of French and Austrian talc workers. *Occup Environ Med*, 59:98–105. doi:10.1136/oem.59.2.98. PMID:11850552
- Wong C, Hempling RE, Piver MS *et al.* (1999). Perineal talc exposure and subsequent epithelial ovarian cancer: a case-control study. *Obstet Gynecol*, 93:372–376. doi:10.1016/S0029-7844(98)00439-6. PMID:10074982
- Wu ML, Whittemore AS, Paffenbarger RS Jr *et al.* (1988). Personal and environmental characteristics related to epithelial ovarian cancer. I. Reproductive and menstrual events and oral contraceptive use. *Am J Epidemiol*, 128:1216–1227. PMID:3195563